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10/032,717	10/23/2001	Andre R. Abad	35718/237005 (5718-118)	5409

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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 05/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,717	ABAD ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9-12,17-19,38-40,43-46,49-52 and 55-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9-12,17-19,38,43,46,49,52 and 55-64* is/are rejected.

7)☒ Claim(s) *39,40,44,45,50 and 51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: search results

DETAILED ACTION

1. Prosecution in this application has been reopened in light of the modified rejections below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claims 1-3, 9-12, 17-19, 38, 43, 46, 49, 52 and 55-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding SEQ ID NO:2 and 10, expression cassettes comprising the nucleic acids, plants and seeds comprising a construct comprising the nucleic acid, and a method of using it to impact a plant pest, does not reasonably provide enablement for any nucleic acid that has 90% identity to SEQ ID NO:1, expression cassettes comprising the nucleic acid, plants and seeds comprising a construct comprising the nucleic acid and a method of using it to impact a plant pest. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 6 May 2005. Applicant's arguments filed 23 February 2006 in a Reply Brief have been fully considered but they are not persuasive.

The claims are broadly drawn to any nucleic acid that has 90%, 93%, 94% or 95% identity to SEQ ID NO:1, expression cassettes comprising the nucleic acids, plants and seeds

comprising constructs comprising the nucleic acids, and a method of using the constructs to impact a plant pest.

The instant specification, however, only provides guidance for methods of assaying the activity of *B. thuringiensis* strain 1218 and lysate against Western corn rootworm and Southern corn rootworm (examples 1 and 2); isolation of crystal protein from the strain and assaying of it for pesticidal activity against western corn rootworm (example 3); identification of two coding regions, *Cry1218-1* and *Cry1218-2* (SEQ ID NO:1 and 3, with SEQ ID NOs:27 and 28 as the genomic clones), isolated by unknown methods, as encoding proteins, SEQ ID NOs:2 and 4, respectively, that have homology to Cry8Ba1 (example 4); production in *E. coli* of truncated proteins, SEQ ID NOs:15 and 17, encoded by SEQ ID NOs:16 and 18, respectively, that are active against southern corn rootworm (example 4); and production of maize-preferred coding sequences of a different truncated version of Cry1218-1 - the nucleic acid is SEQ ID NO:9, which encodes SEQ ID NO:10 (example 5). The specification also teaches making two mutant versions of truncated Cry1218-1 (SEQ ID NO:16), one of which has a truncated N-terminus (comprising amino acids 43-663 of SEQ ID NO:16), and the other in which the 4 amino acid sequence NGSR has been inserted after amino acid 164 - all of these mutant proteins are effective against Colorado potato beetle (example 6) and other mutant proteins (SEQ ID NOs:32, 34, 42 and 46) that have added chymotrypsin cleavage sites - all are more effective against southern and western corn rootworm than Cry1218-1 (example 7). The specification also teaches transformation of maize with SEQ ID NO:9 (examples 8 and 9).

The instant specification fails to provide guidance for nucleic acid that has 90%, 93%, 94% or 95% identity to the full-length of SEQ ID NO:1, expression cassettes comprising the

nucleic acid, plants and seeds comprising a construct comprising the nucleic acid and a method of using it to impact a plant pest.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain Cry8 activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

The specification on pg 28, lines 5-16, suggests making these nucleic acids by making conservative substitutions in the encoded protein. However, making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). The nucleic acids encoding all these mutated proteins, however, would have much greater than 90% identity to the nucleic acids encoding the original protein.

Making amino acid substitutions in *cry* proteins is unpredictable. Each *cry* protein only has activity against one or few insect species (de Maagd et al, 1999, Appl. Environ. Microbiol.

65:4369-4374, see pg 4369, column 1, paragraph 1). Even a single amino acid substitution in a *cry* protein may alter its insecticidal specificity, and toxicity must be determined empirically (Tounsi et al, 2003, J. Appl. Microbiol. 95:23-28; see pg 27, column 2, paragraph 2). For example, a conservative substitution of a lysine for an arginine in a cry11A protein eliminated toxicity to *Aedes aegyptii* but not other pests to which the wild-type protein has toxicity (Angsuthanasombat et al, 2001, J. Biochem. Mol. Biol. 34:402-407, paragraph spanning the columns on pg 405).

The specification, on pg 65, lines 12-14, indicates that the instant SEQ ID NO:1 has homology to GenBank U04365, which is identical to SEQ ID NO:3 of Michaels et al (1996, US Patent 5,554,534). This nucleotide sequence has 85.1% identity to SEQ ID NO:1. The specification, on pg 29, suggests using GenBank U04365 (SEQ ID NO:3 of Michaels et al) as the other nucleic acid in shuffling to create the claimed nucleic acids; however, it encodes a protein with 79.8% identity to the instant SEQ ID NO:2 (see sequence search report). Thus, this sequence cannot be used as guidance for nucleic acids with 90% identity to SEQ ID NO:1 and that encode proteins with 70% identity to SEQ ID NO:2, as encompassed by the full scope of the claims.

Furthermore, SEQ ID NO:3 of Michaels et al is pesticidal for *Cyclocephala borealis* (northern masked chafer) and *Popillia japonica* (Japanese beetle)(column 14, line 46, to column 15, line 2), whereas the instant SEQ ID NO:1 is pesticidal to *Diabrotica longicornis howardi* (southern corn rootworm). Given the teachings of Tounsi et al, de Maagd et al, and Angsuthanasombat et al, one of skill in the art could not even predict for which pests the protein encoded by nucleic acids that have 90% identity to SEQ ID NO:1 would be toxic, and the

specification does not teach which amino acid substitutions must can be made to retain southern corn rootworm pesticidal activity.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids with 90% identity to SEQ ID NO:1 or that hybridizes to SEQ ID NO:1. Making all possible single amino acid substitutions, in an 3621 nucleotide long nucleic acid like that of SEQ ID NO:1 would require making and analyzing 19^{3621} nucleic acids; these nucleic acids would have about 99.99% identity to SEQ ID NO:1. Because nucleic acids that have 90% identity to SEQ ID NO:1 would have up to 362 nucleotide substitutions, many more than 19^{3621} nucleic acids would need to be made and analyzed.

Furthermore, because nucleic acids that have 90% identity to SEQ ID NO:1 would have up to 362 nucleotide substitutions, they could encode proteins with up to 362 amino acid substitutions; these proteins would have 70% identity to the 1206 amino acid long SEQ ID NO:2. The specification provides no guidance for which 362 amino acids to substitute. Thus, undue trial and error experimentation would be required to make the claimed nucleic acids.

Similarly, nucleic acids that have 93% identity to SEQ ID NO:1 would have up to 253 nucleotide substitutions, nucleic acids that have 94% identity to SEQ ID NO:1 would have up to 217 nucleotide substitutions and nucleic acids that have 90% identity to SEQ ID NO:1 would have up to 181 nucleotide substitutions, producing proteins with 79%, 82% and 85% identity, respectively, to the 1206 amino acid long SEQ ID NO:2.

Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of

substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with up to 363 amino acid substitutions that also have pesticidal activity would require undue experimentation.

As the specification does not describe the transformation of any plant with nucleic acids with 90% identity to SEQ ID NO:1 within the full scope of the claims, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those that could control plant pests, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that the specification provides 14 variants of SEQ ID NO:1; these have between 38% and 92% identity across the full-length of SEQ ID NO:1 (Reply Brief pg 3-4 and Table 1).

This is not found persuasive.

First, Applicant has numerous errors in Table 1. The amino acids listed as deleted are not the deleted amino acids; they are the ones still present in the protein. Examiner has not recalculated nucleotide or amino acid identity for the sequences, but it is noted that in Applicant's previous responses, SEQ ID NO:19 was indicated as having different percent global identity to SEQ ID NO:1.

Second, one of skill in the art would not consider a truncated protein as having 56% identity to the entire length of SEQ ID NO:2, but would only look at it as a truncated protein. One of skill in the art would only look at local match similarity. That the specification provides guidance in making truncations at amino acid 663, 699 and 667, eliminating the C-terminus, and truncations off a portion of the N-terminus (in which the first 47 amino acids are eliminated) is not disputed. However, this is not the genus of claimed nucleic acids.

Third, the specification does not consider deletions the same thing as substitutions. See pg 19, lines 3-10 and pg 28, lines 5-31, in which deletions and substitutions are discussed in the alternative.

Fourth, these sequences (except SEQ ID NO:3/4) teach a maximum of 4 amino acid substitutions. One of skill in the art would not consider these sequences as teaching which 181, 217, 253 or 362 amino acids to substitute in SEQ ID NO:2.

Fifth, SEQ ID NO:3 differs from SEQ ID NO:1 in primarily in a 400 nucleotide long region (see search results). Because the vast majority of substitutions are localized to such a small area, the protein it encodes, SEQ ID NO:4 has 89% identity to SEQ ID NO:2. Thus, SEQ ID NO:3 cannot provide guidance for making nucleic acids with 90% identity to SEQ ID NO:1 and encoding a protein with 362 amino acid substitutions relative to SEQ ID NO:2.

In summary, making fragments and a single 4 amino acid substitution are not the same thing as making 362 amino acid substitutions. The specification fails to enable nucleic acids within the full scope of the claims.

Applicant urges that SEQ ID NO:19 comprises 1860 nucleotides of SEQ ID NO:1 and retains identity, pointing to the likelihood that alteration of one or more of the 1761 additional

nucleotides in SEQ ID NO:1 could be altered without disrupting function; furthermore, SEQ ID NO:9 encodes the same protein as SEQ ID NO:19 but has maize optimized codons, and it shares 38% global identity to SEQ ID NO:1 and 68% local identity (Reply Brief pg 4).

This is not found persuasive. SEQ ID NOs:19 and 9 encode proteins with 100% identity to the first half of SEQ ID NO:2. One of skill in the art would not consider a truncated protein as providing guidance for making amino acid substitutions in SEQ ID NO:2. Substitutions in the latter half of the protein affect the folding of the entire protein, and cannot be made willy-nilly just because a protein can be truncated.

Applicant urges that the examiner overlooks the guidance in the specification as to which 362, 253 or 217 nucleotides of SEQ ID NO:1 could be altered; guidance is provided on pg 23-24, 29 and examples 1, 6 and 7 (Reply Brief pg 8).

This is not found persuasive. Pg 23 provided general guidance for methods of making mutations in nucleic acids. It does not provide guidance for which 362 amino acid substitutions to make in SEQ ID NO:2.

Pg 24 teaches that cry proteins have conserved blocks. However, Hill et al teach that conserved blocks cannot be relied on in making amino acid substitutions (see Table 1).

The specification, on pg 29, suggests using GenBank U04365 as the other nucleic acid in shuffling to create the claimed nucleic acids; however, it encodes a protein with 79.8% identity to the instant SEQ ID NO:2. Thus, this sequence cannot be used as guidance for nucleic acids with 90% identity to SEQ ID NO:1 and that encode proteins with 70% identity to SEQ ID NO:2, as encompassed by the full scope of the claims.

Furthermore, SEQ ID NO:3 of Michaels et al is pesticidal for scarab pests (see claim 1),

whereas the instant SEQ ID NO:1 is pesticidal to southern corn rootworm. Given the teachings of Tounsi et al, de Maagd et al, and Angsuthanasombat et al, one of skill in the art could not even predict for which pests the protein encoded by nucleic acids that have 90% identity to SEQ ID NO:1 would be toxic, and the specification does not teach which amino acid substitutions made to retain proper pesticidal activity.

Examples 1, 6 and 7 teach making the truncations and the 4 amino acid substitutions presented in Table 1 of the Reply Brief. Why these examples do not teach nucleic acids within the full scope of the claims is discussed above.

Making amino acid substitutions in *cry* proteins is unpredictable. Even a single amino acid substitution in a *cry* protein may alter its insecticidal specificity, and toxicity must be determined empirically (Tounsi et al, 2003, J. Appl. Microbiol. 95:23-28; see pg 27, column 2, paragraph 2). Thus the specification must teach how to make nucleic acids within the full scope of the claims. It does not.

The specification on pg 3, lines 4-8, even acknowledges the unpredictability in making amino acid substitutions in Cry proteins:

> Although numerous investigators have attempted to make mutant endotoxin proteins with improved insecticidal activity, few have succeeded. In fact, the majority of genetically engineered B. thuringiensis toxins that have been reported in the literature report endotoxin activity that is no better than that of the wild-type protein, and in many cases, the activity is decreased or destroyed altogether.

Applicant urges that the examiner overlooks the guidance in Li et al, as citing on pg 25 of the specification, and Applicant's data on the truncated proteins (Reply Brief pg 8-10).

This is not found persuasive. The guidance in Li et al was not overlooked. However, Li et al only provided guidance for making truncations and insertion of chymotrypsin cleavage sites; Li et al do not provide guidance for making 181, 217, 253 or 362 amino acid substitutions

in a 1206 amino acid protein. The instant inventors did not use Li et al to make 181, 217, 253 or 362 amino acid substitutions in a 1206 amino acid protein to create a Coleopteran pesticidal protein. Furthermore, truncated proteins are not the same as substituted proteins, as discussed above.

Applicant urges that some experimentation would be necessary to make and use other embodiments of the invention, but it would not be undue, given the guidance in the specification (Reply Brief pg 10-11).

This is not found persuasive. Such experimentation would be undue because of the lack of guidance in the specification and the unpredictability in making amino acid substitutions in *cry* proteins. See the specification on pg 3, lines 4-8, as well as Tounsi et al, de Maagd et al, and Angsuthanasombat et al, as discussed above.

Applicant urges that Lazar is drawn to a mammalian protein unrelated to the instant Cry protein, and the amino acids modified in that paper were known to be conserved, unsurprisingly leading to a loss of function (Reply Brief pg 11-12).

This is not found persuasive. Lazar et al was testing the commonly accepted notion that making conservative substitutions would not affect activity and that nonconservative substitutions would affect activity, even inactivate the protein. Lazar et al were surprised to find that this was not the case - conservative substitutions inactivated the protein and nonconservative substitutions has no effect on activity. This is relevant to the instant case because the specification, on pg 28, lines 5-16, teaches that amino acid substitutions should be conservative. Lazar et al teaches that functional substitutions must be determined empirically. The specification does teach which substitutions to make within the full scope of the claims.

Applicant urges that Hill et al is drawn to an enzyme unrelated to the instant Cry protein, and the modified residues were highly conserved, unsurprisingly leading to a loss of function (Reply Brief pg 12-13).

This is not found persuasive. Hill et al was testing the commonly accepted notion that amino acids conserved across proteins from a wide range of species can only tolerate conservative substitutions if they can tolerate any at all. Hill et al were surprised to find that this was not the case - nonconservative substitutions had no effect on activity and conservative substitutions inactivated the protein. This is relevant to the instant case because the specification, on pg 28, lines 5-16, teaches that amino acid substitutions should be conservative and on pg 24-25 teaches that other cry proteins can be used as comparisons when making the claimed nucleic acids. Hill et al teaches that functional substitutions must be determined empirically. The specification does teach which substitutions to make within the full scope of the claims.

Applicant urges that Lazar et al and Hill et al demonstrate that one of skill in the art could make substitutions in proteins and test for activity (Reply Brief pg 13).

This is not found persuasive. Lazar et al and Hill et al made single amino acid substitutions. The claims encompass nucleic acids that having 90% identity to SEQ ID NO:1 and encoding functional Cry proteins with 362 amino acid substitutions. Guo et al teaches that increasing the number of substitutions above single amino acid changes additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, without further guidance, one of skill in the art could not make this many substitutions and still produce functional proteins.

Applicant urges that there is guidance in the specification for making modifications (Reply Brief pg 13).

This is not found persuasive because the specification fails to provide guidance for making nucleic acids that having 90% identity to SEQ ID NO:1 and encoding functional Cry proteins with 362 amino acid substitutions, as encompassed by the full scope of the claims.

4. Claims 1-3, 9-12, 17-19, 38, 43, 46, 49, 52 and 55-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 6 May 2005. Applicant's arguments filed 23 February 2006 in a Reply Brief have been fully considered but they are not persuasive.

A full review of the specification indicates that nucleic acids that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1 and that encode Coleopteran-pesticides are essential to the operation of the claimed invention.

The level of skill and knowledge in the art at the time of filing was such that while large number of Coleopteran-pesticides were known, nucleic acids that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1 and that encode such Coleopteran-pesticides were not.

The claim is directed to a genus of nucleic acids that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1. Nucleic acids that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1 would have up to 362 nucleotide substitutions, they could encode proteins with up to 362,

253, 217 or 181 amino acid substitutions relative to the to the 1206 amino acid long SEQ ID NO:2.

The structural features that distinguish Coleopteran-pesticide-encoding nucleic acids that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1 from other that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1 are not described in the specification. The specification recites no structure required for Coleopteran-pesticide activity. The necessary and sufficient structural elements of a protein with Coleopteran-pesticide activity are not described.

The only species described in the specification is SEQ ID NO:1, which encodes SEQ ID NO:2, a truncated version of SEQ ID NO:1, and a few nucleic acids with a few nucleotide substitutions relative to SEQ ID NO:1.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1 alone is insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described nucleic acids with 90%, 93%, 94% or 95% identity to SEQ ID NO:1 and that encode a protein pesticidal for at least one pest belonging to the order Coleoptera within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

Applicant urges that the specification provides numerous nucleic acids that fall within the scope of the claims as well as much guidance for making alterations (Reply Brief pg 15).

This is not found persuasive because the structure of nucleic acids that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1 and up to 362, 253, 217 or 181 amino acid substitutions, respectively, relative to the to the 1206 amino acid long SEQ ID NO:2 as encompassed by the full scope of the claims are not described.

Applicant urges that in *Lilly* the patent did not identify the sequence of any embodiment, while here a representative sequence is provided (Reply Brief pg 15).

This is not found persuasive. In *Lilly* the claims were drawn to the genus of vertebrate and mammalian cDNAs and the rat cDNA was described. Lilly stated at pg 1406:

> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

In the instant case, only a portion of the structural features have been described - the percent identity to SEQ ID NO:1. But because this includes nucleic acids in which the protein sequence has a very large number of amino acid substitutions, those amino acid substitutions that do not alter the function of the protein must be described. They are not. A representative number of nucleic acids that have 90%, 93%, 94% or 95% identity to SEQ ID NO:1 and up to 362, 253, 217 or 181 amino acid substitutions, respectively, relative to the to the 1206 amino acid long SEQ ID NO:2 are not described.

5. Claims 39-40, 44-45 and 50-51 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Anne Kubelik, Ph.D.
April 28, 2006

ANNE KUBELIK, PH.D.
PRIMARY EXAMINER

ANNE MARIE GRUNBERG
SUPERVISORY PATENT EXAMINER

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Db   3191 ATTCGTCATCAAACGAACCGAATTGTAAAAAATGTACCGGATGATTTGCTGCCAGATGTA 3250

Qy   2521 TCTCCTGTTAACTCGGATGGTAGTATCAATCGATGCAGCGAACAAAAGTATGTGAATAGC 2580
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3251 TCTCCTGTTAACTCGGATGGTAGTATCAATCGATGCAGCGAACAAAAGTATGTGAATAGC 3310

Qy   2581 CGTTTAGAAGTAGAAAACCGTTCTGGTGAAGCGCATGAGTTCTCTATTCCTATTGATACA 2640
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3311 CGTTTAGAAGTAGAAAACCGTTCTGGTGAAGCGCATGAGTTCTCTATTCCTATTGATACA 3370

Qy   2641 GGTGAAATCGATTACAATGAAAATGCAGGAATATGGGTTGGATTTAAGATTACGGACCCA 2700
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3371 GGTGAAATCGATTACAATGAAAATGCAGGAATATGGGTTGGATTTAAGATTACGGACCCA 3430

Qy   2701 GAGGGATATGCAACACTCGGAAACCTAGAATTGGTCGAAGAGGGACCTTTATCAGGAGAC 2760
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3431 GAGGGATATGCAACACTCGGAAACCTAGAATTGGTCGAAGAGGGACCTTTATCAGGAGAC 3490

Qy   2761 GCATTAGAACGCTTGCAAAGAGAAGAACAACAGTGGAAGATTCAAATGACAAGAAGACGT 2820
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3491 GCATTAGAACGCTTGCAAAGAGAAGAACAACAGTGGAAGATTCAAATGACAAGAAGACGT 3550

Qy   2821 GAAGAAACAGATAGAAGGTATATGGCATCGAAACAAGCGGTAGATCGTTTATATGCCGAT 2880
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Db   3551 GAAGAAACAGATAGAAGGTATATGGCATCGAAACAAGCGGTAGATCGTTTATATGCCGAT 3610

Qy   2881 TATCAGGATCAGCAACTGAATCCTGATGTAGAGATTACAGATCTTACTGCGGCCCAAGAT 2940
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Db   3611 TATCAGGATCAGCAACTGAATCCTGATGTAGAGATTACAGATCTTACTGCGGCCCAAGAT 3670

Qy   2941 CTGATACAGTCCATTCCTTACGTATATAACGAAATGTTCCCAGAAATACCAGGGATGAAC 3000
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Qy   3001 TATACGAAGTTTACAGAATTAACAGATCGACTCCAACAAGCGTGGAGTTTGTATGATCAG 3060
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3731 TATACGAAGTTTACAGAATTAACAGATCGACTCCAACAAGCGTGGAGTTTGTATGATCAG 3790

Qy   3061 CGAAATGCCATACCAAATGGTGATTTTCGAAATGGGTTAAGTAATTGGAATGCAACGCCT 3120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3791 CGAAATGCCATACCAAATGGTGATTTTCGAAATGGGTTAAGTAATTGGAATGCAACGCCT 3850

Qy   3121 GGCGTAGAAGTACAACAAATCAATCATACATCTGTCCTTGTGATTCCAAACTGGGATGAG 3180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3851 GGCGTAGAAGTACAACAAATCAATCATACATCTGTCCTTGTGATTCCAAACTGGGATGAG 3910

Qy   3181 CAAGTTTCGCAACAGTTTACAGTTCAACCGAATCAAAGATATGTGTTACGAGTTACTGCG 3240
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Db   3911 CAAGTTTCGCAACAGTTTACAGTTCAACCGAATCAAAGATATGTGTTACGAGTTACTGCG 3970

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          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   3971 AGAAAAGAAGGGGTAGGAAATGGATATGTAAGTATCCGTGATGGTGGAAATCAAACAGAA 4030

Qy   3301 ACGCTTACTTTTAGTGCAAGCGATTATGATACAAATGGAATGTATAATACGCAAGTGTCC 3360
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4031 ACGCTTACTTTTAGTGCAAGCGATTATGATACAAATGGAATGTATAATACGCAAGTGTCC 4090

Qy   3361 AATACAAATGGATATAACACAAATAATGCGTATAATACACAAGCATCGAGTACAAACGGA 3420
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4091 AATACAAATGGATATAACACAAATAATGCGTATAATACACAAGCATCGAGTACAAACGGA 4150

Qy   3421 TATAACGCAAATAATATGTATAATACGCAAGCATCGAATACAAACGGATATAACACAAAT 3480
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Db   4151 TATAACGCAAATAATATGTATAATACGCAAGCATCGAATACAAACGGATATAACACAAAT 4210

Qy   3481 AGTGTGTACAATGATCAAACCGGCTATATCACAAAAACAGTGACATTCATCCCGTATACA 3540
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4211 AGTGTGTACAATGATCAAACCGGCTATATCACAAAAACAGTGACATTCATCCCGTATACA 4270

Qy   3541 GATCAAATGTGGATTGAGATGAGTGAGACAGAAGGTACATTCTATATAGAAAGTGTAGAA 3600
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Db   4271 GATCAAATGTGGATTGAGATGAGTGAGACAGAAGGTACATTCTATATAGAAAGTGTAGAA 4330

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Db   4331 TTGATTGTAGACGTAGAGTAA 4351
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RESULT 3
US-10-032-717-3
; Sequence 3, Application US/10032717
; Patent No. US20020151709A1
; GENERAL INFORMATION:
;  APPLICANT: Andre R. Abad
;  APPLICANT:  Nicholas B. Duck
;  APPLICANT:  Xiang Peng
;  APPLICANT:  Ronald D. Flannagan
;  APPLICANT:  Theodore W. Kahn
;  APPLICANT:  Lynn E. Sims
;  TITLE OF INVENTION: Genes Encoding No. US20020151709A1el Proteins With
;  TITLE OF INVENTION:  Pesticidal Activity Against Coleopterans
;  FILE REFERENCE: 35718/237005
;  CURRENT APPLICATION NUMBER: US/10/032,717
;  CURRENT FILING DATE:  2001-10-23
;  PRIOR APPLICATION NUMBER: 60/242,838
;  PRIOR FILING DATE: 2000-10-24
;  NUMBER OF SEQ ID NOS: 48
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 3
;   LENGTH: 3633
;   TYPE: DNA
;   ORGANISM: Bacillus thuringiensis
;   FEATURE:
;   NAME/KEY: CDS
;   LOCATION: (1)...(3633)
;   NAME/KEY: misc_feature
;   LOCATION: (0)...(0)
;   OTHER INFORMATION: Cry1218-2
US-10-032-717-3

  Query Match            87.0%;  Score 3151.8;  DB 12;  Length 3633;
  Best Local Similarity  92.1%;  Pred. No. 0;
  Matches 3353;  Conservative    0;  Mismatches  262;  Indels   24;  Gaps    2;

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Qy     121 GATTATAAAGATTATTTAAAAATGTCTGCGGGAAATGCTAGTGAATACCCTGGTTCACCT 180
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Db     121 GATTATAAAGATTATTTAAAAATGTCTGCGGGAAATGCTAGTGAATACCCTGGTTCACCT 180

Qy     181 GAAGTACTTGTTAGCGGACAAGATGCAGCTAAGGCCGCAATTGATATAGTAGGTAAATTA 240
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Db     181 GAAGTACTTGTTAGCGGACAAGATGCAGCTAAGGCCGCAATTGATATAGTAGGTAAATTA 240

Qy     241 CTATCAGGTTTAGGGGTCCCATTTGTTGGGCCGATAGTGAGTCTTTATACTCAACTTATT 300
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Db     241 CTATCAGGTTTAGGGGTCCCATTTGTTGGGCCGATAGTGAGTCTTTATACTCAACTTATT 300

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Db     301 GATATTCTGTGGCCTTCAGGGCAAAAGAGTCAATGGGAGATTTTTATGGAACAAGTAGAA 360

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Qy     421 GGATTAGGTAATAATTACCAATTATATCTAACTGCGCTTGAAGAATGGGAAGAAAATCCA 480
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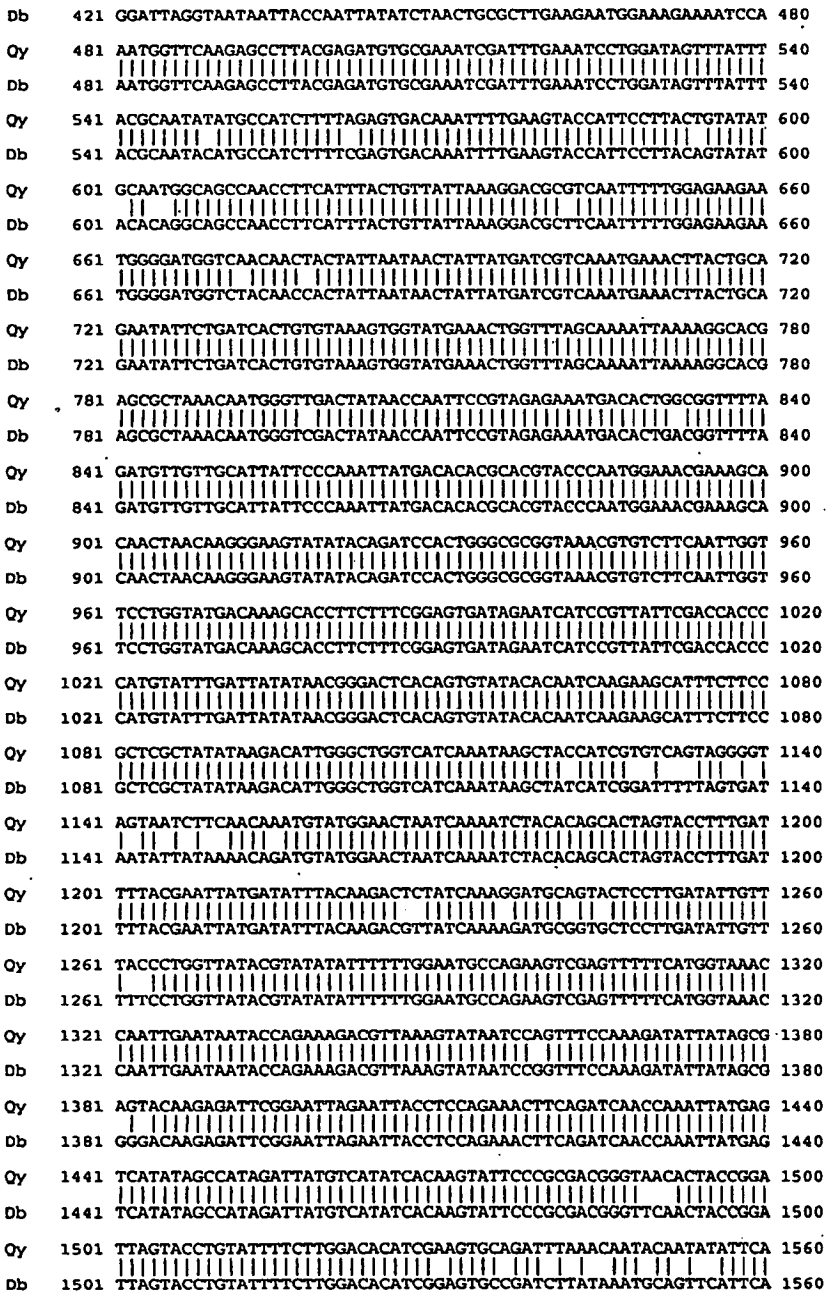
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Qy 661 TGGGGATGGTCAACAACTACTATTAATAACTATTATGATCGTCAAATGAAACTTACTGCA 720
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Qy 721 GAATATTCTGATCACTGTGTAAAGTGGTATGAAACTGGTTTAGCAAAATTAAAAGGCACG 780
Db 721 GAATATTCTGATCACTGTGTAAAGTGGTATGAAACTGGTTTAGCAAAATTAAAAGGCACG 780
Qy 781 AGCGCTAAACAATGGGTTGACTATAACCAATTCCGTAGAGAAATGACACTGGCGGTTTTA 840
Db 781 AGCGCTAAACAATGGGTCGACTATAACCAATTCCGTAGAGAAATGACACTGACGGTTTTA 840
Qy 841 GATGTTGTTGCATTATTCCCAAATTATGACACACGCACGTACCCAATGGAAACGAAAGCA 900
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Qy 1381 AGTACAAGAGATTCGGAATTAGAATTACCTCCAGAAACTTCAGATCAACCAAATTATGAG 1440
Db 1381 GGGACAAGAGATTCGGAATTAGAATTACCTCCAGAAACTTCAGATCAACCAAATTATGAG 1440
Qy 1441 TCATATAGCCATAGATTATGTCATATCACAAGTATTCCCGCGACGGGTAACACTACCGGA 1500
Db 1441 TCATATAGCCATAGATTATGTCATATCACAAGTATTCCCGCGACGGGTTCAACTACCGGA 1500
Qy 1501 TTAGTACCTGTATTTTCTTGGACACATCGGAAGTGCAGATTTAAACAATACAATATATTCA 1560
Db 1501 TTAGTACCTGTATTTTCTTGGACACATCGGAGTGCCGATCTTATAAATGCAGTTCATTCA 1560
Qy 1561 GATAAAATCACTCAAATTCCGGCCGTTAAATGTTGGGATAATTTACCGTTTGT------- 1613
Db 1561 GATAAAATTACTCAGATTCCGGTCGTAAAGGTTTCTGATTTGGCTCCCTCTATAACAGGA 1620
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Db 1621 GGGCCAAATAATACCGTTGTATCGGGTCCTGGATTTACAGGGGGGGGGATAATAAAAGTA 1680
Qy 1663 AATAGAAGTACTGGTTCTGTAGGAACCTTATTTCTAGCTCGATATGGCCTAGCATTAGAA 1722
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Qy 1723 AAAGCAGGGAAATATCGTGTAAGACTGAGATATGCTACTGATGCAGATATTGTATTGCAT 1782
Db 1741 TATAGTATGAGGATTCGGTATGCTTCCGCTAATAATACTGAATTTTATATAAATCCTTCT 1800
Qy 1783 GTAAACGATGCTCAGATTCAGATGCCAAAAACAATGAACCCAGGTGAGGATCTGACATCT 1842
Db 1801 GAAGAAAACGTTAAATCTCACGCTCAAAAAACTATGAATAGAGGTGAAGCTTTAACATAT 1860
Qy 1843 AAAACTTTTAAAGTTGCAGATGCTATCACAACATTAAATTTAGCAACAGATAGTTCGCTA 1902
Db 1861 AATAAATTTAATTATGCGACTTTGCCCCCTATTAAATTTACGACAACCGAACCTTTCATT 1920
Qy 1903 GCATTGAAACATAATTTAGGTGAAGACCCTAATTCAACATTATCTGGTATAGTTTACGTT 1962
Db 1921 ACTCTAGGGGCTATATTTGAAGCGGAAGACTTTCTTGGAAT------TGAAGCTTATATA 1974
Qy 1963 GACCGAATCGAATTCATCCCAGTAGATGAGACATATGAAGCGGAACAAGATTTAGAAGCA 2022
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Qy 2083 ACGGATTATGAAGTGAATCAAGCGGCAAACTTAGTGGAATGCCTATCGGATGATTTGTAT 2142
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Qy 2203 CGTAATTTGCTTCAAGATCCAGATTTCCAAGAGATAAATGGAGAAAATGGCTGGACGGCA 2262
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Qy 2263 AGTACGGGAATTGAGGTTATAGAAGGGGATGCTTTATTCAAAGGGCGTTATCTACGCCTA 2322
Db 2275 AGTACGGGAATTGAGGTTATAGAAGGGGATGCTTTATTCAAAGGGCGTTATCTACGCCTA 2334
Qy 2323 CCAGGTGCGAGAGAAATAGATACGGAAACGTATCCAACGTATCTGTATCAAAAAGTAGAG 2382
Db 2335 CCAGGTGCGAGAGAAATAGATACGGAAACGTATCCAACGTATCTGTATCAAAAAGTAGAG 2394
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Db 2395 GAAGGTGTATTAAAACCATACACAAGATATAGATTGAGAGGGTTTGTCGGAAGCAGTCAA 2454
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Db   2635 TCTATTCCTATTGATACAGGTGAAATCGATTACAATGAAAATGCAGGAATATGGGTTGGA 2694

Qy   2683 TTTAAGATTACGGACCCAGAGGGATATGCAACACTCGGAAACCTAGAATTGGTCGAAGAG 2742
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Db   2695 TTTAAGATTACGGACCCAGAGGGATATGCAACACTCGGAAACCTAGAATTGGTCGAAGAG 2754

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Qy   2863 GATCGTTTATATGCCGATTATCAGGATCAGCAACTGAATCCTGATGTAGAGATTACAGAT 2922
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Db   3235 GTGTTACGAGTTACTGCGAGAAAAGAAGGGGTAGGAAATGGATATGTAAGTATCCGTGAT 3294

Qy   3283 GGTGGAAATCAAACAGAAACGCTTACTTTTAGTGCAAGCGATTATGATACAAATGGAATG 3342
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Db   3295 GGTGGAAATCAAACAGAAACGCTTACTTTTAGTGCAAGCGATTATGATACAAATGGAATG 3354

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Db   3355 TATAATACGCAAGTGTCCAATACAAATGGATATAACACAAATAATGCGTATAATACACAA 3414

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RESULT 4
US-10-032-717-28
; Sequence 28, Application US/10032717
; Patent No. US20020151709A1

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; GENERAL INFORMATION:
;  APPLICANT: Andre R. Abad
;  APPLICANT:  Nicholas B. Duck
;  APPLICANT:  Xiang Feng
;  APPLICANT:  Ronald D. Flannagan
;  APPLICANT:  Theodore W. Kahn
;  APPLICANT:  Lynn E. Sims
;  TITLE OF INVENTION: Genes Encoding No. US20020151709A1el Proteins With
;  TITLE OF INVENTION:  Pesticidal Activity Against Coleopterans
;  FILE REFERENCE: 35718/237005
;  CURRENT APPLICATION NUMBER: US/10/032,717
;  CURRENT FILING DATE:  2001-10-23
;  PRIOR APPLICATION NUMBER: 60/242,838
;  PRIOR FILING DATE: 2000-10-24
;  NUMBER OF SEQ ID NOS: 48
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 28
;   LENGTH: 6613
;   TYPE: DNA
;   ORGANISM: Bacillus thuringiensis
;   FEATURE:
;   NAME/KEY: misc_feature
;   LOCATION: (0)...(0)
;   OTHER INFORMATION: Genomic Cry1218-2
US-10-032-717-28

  Query Match             87.0%;  Score 3151.8;  DB 12;  Length 6613;
  Best Local Similarity   92.1%;  Pred. No. 0;
  Matches 3353;  Conservative    0;  Mismatches  262;  Indels   24;  Gaps    2;

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          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1374 GATTATAAAGATTATTTAAAAATGTCTGCGGGAAATGCTAGTGAATACCCTGGTTCACCT 1433

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Db   1494 CTATCAGGTTTAGGGGTCCCATTTGTTGGGCCGATAGTGAGTCTTTATACTCAACTTATT 1553

Qy    301 GATATTCTGTGGCCTTCAGGGGAAAAGAGTCAATGGGAAATTTTTATGGAACAAGTAGAA 360
          |||||||||||||||||| |||||||||||||||| ||||||||||||||||||||||||
Db   1554 GATATTCTGTGGCCTTCAGGGCAAAAGAGTCAATGGGAGATTTTTATGGAACAAGTAGAA 1613

Qy    361 GAACTCATTAATCAAAAAATAGCAGAATATGCAAGGAATAAAGCGCTTTCGGAATTAGAA 420
          |||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1614 GAACTCATAAATCAAAAAATAGCAGAATATGCAAGGAATAAAGCGCTTTCGGAATTAGAA 1673

Qy    421 GGATTAGGTAATAATTACCAATTATATCTAACTGCGCTTGAAGAATGGGAAGAAAATCCA 480
          |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Db   1674 GGATTAGGTAATAATTACCAATTATATCTAACTGCGCTTGAAGAATGGAAAGAAAATCCA 1733

Qy    481 AATGGTTCAAGAGCCTTACGAGATGTGCGAAATCGATTTGAAATCCTGGATAGTTTATTT 540
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1734 AATGGTTCAAGAGCCTTACGAGATGTGCGAAATCGATTTGAAATCCTGGATAGTTTATTT 1793

Qy    541 ACGCAATATATGCCATCTTTTAGAGTGACAAATTTTGAAGTACCATTCCTTACTGTATAT 600
          |||||||| |||||||||||| |||||||||||||||||||||||||||| ||||||||
Db   1794 ACGCAATACATGCCATCTTTTCGAGTGACAAATTTTGAAGTACCATTCCTTACAGTATAT 1853

Qy    601 GCAATGGCAGCCAACCTTCATTTACTGTTATTAAAGGACGCGTCAATTTTTGGAGAAGAA 660
          ||  ||||||||||||||||||||||||||||||||||||| ||||||||||||||||||
Db   1854 ACACAGGCAGCCAACCTTCATTTACTGTTATTAAAGGACGCTTCAATTTTTGGAGAAGAA 1913
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